NEUROPHYSIOLOGICAL TESTS IN NEUROLUPUS

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SUMMARY

The difficulties in assessing the Central Nervous System (CNS) in the course of Systemic Nervous System (SLE) are well known. A battery of Neurophysiological tests, including EEG and Multimodal Evoked Potencials was used in order to evaluate CNS disfuntion. Two SLE populations were studied (one with previous neurological symptoms (N = 10) and another without any of the these symptoms (N = 10) and compared with normal controls (N = 14). Tests included Routine EEG, Visual Evoked Potencials (VEP), Flash Evoked Responses (FEP), Auditory P300 (P300) and a Reitan B Test. Both SLE populations showed rather high incidences of abnormalities in FEP and VEP; EEG and P300 had smaller percentages of abnormal records. In spite of stronger and more frequent abnormalities in patient with major symptoms in their past the two SLE could not be differentiated in terms of incidence of abnormal Evoked Potencials Records. Visual Evoked Potencials seem a promising method for the assessment of CNS system disfunction SLE patients.

RESUMO

Testes Neurofisiológicos no LED

As dificuldades existentes quanto à avaliação do envolvimento do Sistema Nervoso Central (CNS) no curso do Lupus Eritmatoso Disseminado (LED) são bem conhecidas de todos. Com o objectivo de se avaliarem as alterações do Sistema Nervoso Central (CNS) nestes casos foi utilizada uma bateria de testes neurofisiológicos incluindo Electroencefalograma e Potenciais Evocados Multimodais. Foram estudadas duas populações de Lupus Eritematoso Sistémico, uma com sintomas neurológicos prévios (N = 10) e uma outra sem nenhum sintoma deste tipo (N = 10), e comparadas com controles normais (N = 14). Os testes incluiram EEG de rotina, Potenciais Evocados Visuais (VEP), FEP, P300 Auditivo e um Reitan B Teste. As duas populações estudadas mostraram altas incidências de anomalias nos FEP e nos VEP. O EEG e o P300 mostraram percentagens menores de registos anormais. Apesar de serem mais marcadas e mais frequentes as anomalias em doentes com sintomas major, as duas populações de LED não poderam ser diferenciadas em termos de incidência de registos anormais de Potenciais Evocados. Os Potenciais Evocados Visuais parecem constituir um método promissor em termos de avaliação das disfunções do Sistema Nervoso Central (CNS) no decurso do LED.

INTRODUCTION

Cerebral involvment in systemic Lupus Erythematosus (SLE) occurs frequently and worsens patients prognosis. The most frequent neurological manifestations are convulsions, motor or sensorial deficits, altered states of consciousness, organic cerebral syndrome, intracranial hypertension and persistent headaches. Psychiatry symptoms include psychotic states, depression, cognitive deficits and behaviour disturbances. Diagnosis of neurolupus, on account of prognostic reasons, is essential. Clinical diagnosis is, however, difficult in cases where symptoms may be confused with psychiatric manifestations in relation to the caracteristics of the disease. So far several methods have been used in order to detect Lupus of the Central Nervous System (CNS). Anti DNA antibodies [1] standard cerebral cintigraphy [2], CT Scan [3] and routine Electroencephalogram (EEG) [4] did not provide sufficient diagnostic accuracy [5]. Cerebral cintigraphy using 015 gives more specific results in this subject, but is unsuited for routine use.

OBJECTIVES

1) Evaluation of abnormalities of multimodal Evoked Potencial (EP) and EEG in Neurolupus.
2) Comparison with 2 control populations: one without any symptom of eventual CNS involvment, one normal control population.

MATERIAL AND METHODS

Population

Two groups of patients with SLE were choosen:
— Group 1 (L1) — patients without any CNS symptoms; N

Recebido para publicação: 1 de Março de 1987

= 10; Mean age = 45.83 +/- 14.0; All females.

— Group 2 (L2) — patients with neurological symptoms in their past, but stable in the six months preceding the study. Patients had one or more of the following manifestations: convulsions, paralysis, cranial nerve involvment, aphasia, ataxia and organic cerebral syndrome; N 10; Mean age = 45.26 +/- 13.71; All females.

— Control Group (NO) — A control population of normal individuals included 14 subjects; Mean age = 47.51 +/- 13.12 (8 males and 6 females).

Experimental Design

All groups performed a series of tests that included:

— Routine EEG with eyes closed and hyperventilation

— Visual Evoked Responses — VEP — (pattern reversal, full field) with check's visual angle of 15'. Dimension of the screen was 32×24 cm and distances 115 cm; black level — 0.5 ev, white level 8.0 ev.

— Flash Evoked Responses — FEP — induced by a flash stimulator with simulus intensity of 0.5 Joules (white light).

- Autitory P300 by delivering a random series of 2000 (15%) and 1000 Hz (85%), with an interstimulus interval between 1 to 1.5 sec., the task being the mental count of the rare stimuli. Two trials with trigger on the «true» stimulus and one with trigger on the «false» stimulus were performed.

— Performance of a Reitan B test.

Recordings used a 16 channels EEG machine (Siemens Mingograf EEG 21).

Settings for neurophysiological tests were as follows: filter 30 Hz, time constant 0.3 sec., amplification 100 microvolts/cm. Linked ear was used as reference; 10-20 system electrode position was choosen, namely F4, F3, F8, F7, C4, C3, T6, T5, P4, P3, 02, 01, Fz, Cz, Pz and Oz. Data were transfered to a computer (LSI 11-2), which also controlled the EEG settings; sampling frequency was 1.0 HKz; N. of Epochs: 128 for VEP's, 64 for P300; Repetition Rate 0.5 per sec. Average of EP used saturation level for artefact rejection. Mapping of EP used an interpolation matrix of potencial amplitude at choosen instants of time. Graphic displayed 16 levels of potencial's amplitudes.

All tests, for each subject, were performed on the same day.

3 — Data evaluation

By visual inspection abnormality criteria were defined as follows;

— For Visual Evoked Potencials (VEP and FEP) the response was considered abnormal whenever increased latencies or distorted waveforms were present.

— For P300 abnormality was present when the response to the true stimulus had increased latency or was absent, or when there was a response to the false stimulus [6].

Furthermore peaks were detected where the responses was expected to be maximal, in Oz for Visual Evoked Potencials and Cz for The P300; and automatic computation of peak latency for the relevant channel and of amplitudes at that moment in all the other channels was processed and storedy by software.

4 — Statistical methods

Percentages of abnormalities in the population tested were evaluated using contingency analysis. Contingency tables and computation of correlation coefficients were used to access eventual correlations among the tests used.

In measurements of amplitude and latency of evoked potencials one way analysis of variance was used.

RESULTS

1) Pattern reversal evoked potentials

VEP's were abnormal in 10% of the patients from L1 group and in 56% of those from L2 group. An example is shown in fig. 1. Peak latencies were not different when the 3 population were compared (Table I).

However peak amplitudes in patients (group L1 and L2) were significantly higher than those if normal controls in the frontal derivations, mostly for P1 and N2 (see Fig. 2).

TABLE I

VEP latencies

		L1	L2	NO
N1	A	105.50	98.67	96.00
	SD	16.36	7.45	5.56
P1	A	124.00	119.33	124.4
	SD	18.24	3.27	6.17
N2	A	148.84	157.50	158.55
	SD	9.95	10.78	9.88
P2	A	208.00	201.43	205.00
	SD	22.33	9.85	13.55

No significant differences among L1/L2; L1/NO and L2/NO.
A = Average; SD = Standard Deviation

2) Flash evoked potentials

FEP were abnormal in both patient populations (L1 100%; L2 88%). An example is shown in Fig. 3.

Delayed peak latencies were the commonest feature of the L2 group, which could be distinguished from controls and L1 patients (see Table II).

TABLE II

FEP latencies

		LI	L2	NO
N1	A	86.75	87.71	87.83
	SD	16.14	14.08	5.62
P1	A	116.50	131.78 * * * *	116.83
	SD	22.16	10.74	7.10
N2	A	148.00	173.78 * * * *	148.36
	SD	28.11	19.63	14.88
P2	A	180.86	208.44 * * * * *	158.25
	SD	21.96	25.58	19.34

No significant differences among L1/NO.
Levels of confidence inserted for comparision between L2/NO: * * * * $p > 0.005$
* * * * * $p > 0.001$
A = Average; SD = Standard deviation

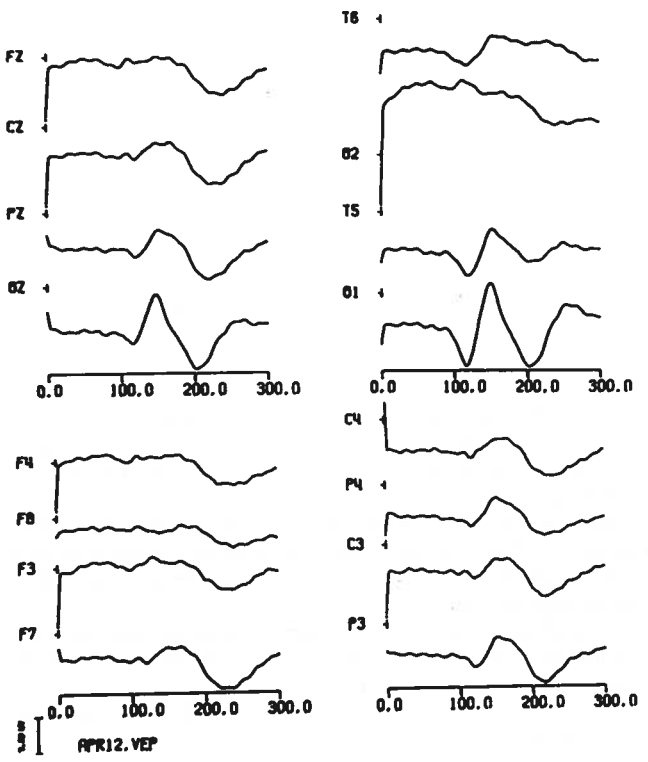

Figure 1 Pattern Reversal Evoked Potencials from a patient. Note the marked abnormality of the waveform

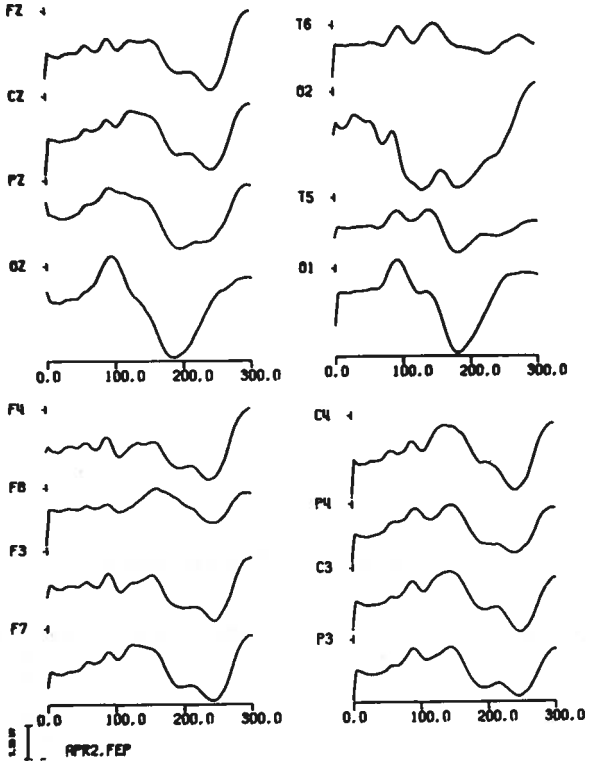

Figure 3 Abnormal Flash Evoked in SLE patient

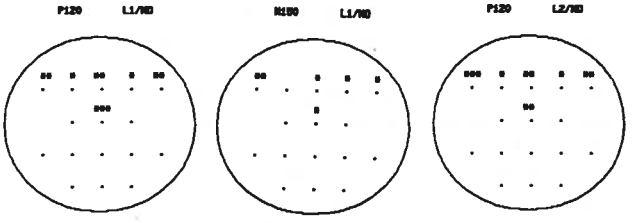

Figure 2 Display of the representative values for VEP peak amplitudes. Frontal accentuation is observed; * represents values significantly different from the control population.
* $p > .05$ and ** $p > .025$

3) P300

The P300 responses were abnormal in 33% of the patients from L1 group and in 22% of patients from L2 group.

The latency of P300 component was also not different from the normal controls, as shown below.

	L1	L2	NO
Mean	248.00	258.86	243.45
St. Dev.	31.67	19.79	29.81

4) EEG

Routine EEG was abnormal in 40% of the patients of group L1 and in 56% of patients of group L2.

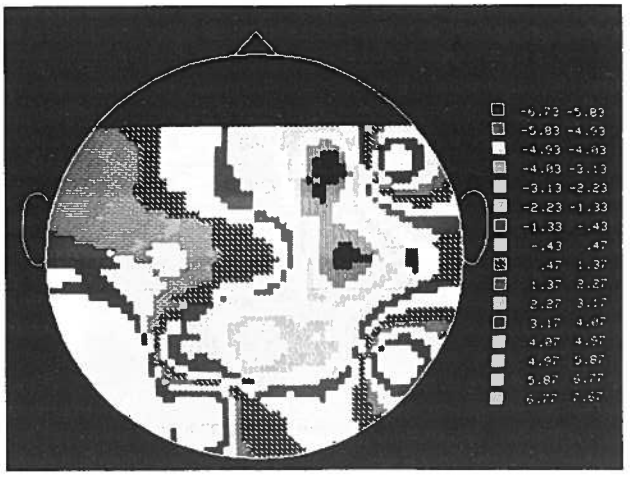

Figure 4 Abnormal Mapping of P300 responses Note the marked asymetry.

Abnormalities were mostly slowing of the background activity and paroxysmal activity in the temporal or rolandic regions.

5) Reitan B Test

It was abnormal in 13% of L1 patients in 23% of L2 patients, and in 0% the normal controls.

6) Comparison between methods

Table III shows per each group, the classification of records on basis of visual inspection, with the respective percentages of abnormality. The chi square values resulting from a contingency analysis are also presentde for the comparison among groups.

FEP, VEP and EEG are more frequently abnormal in the patient populations than in normals. No differences were detected in the Reitan Tests performance and in P300 responses.

Results of a contingency table for correlation among methods are presented in table IV.

In group L1 an inverse correlation between abnormal VEP's and normal Reitan Test performance was detected.

In group L2 correlations between VEP/FEP and VEP/EEG abnormalities were found; and inverse correlations between abhormal FEP and normal Reitan Test was also detected.

TABLE III

A — Incidence of abnormal records

LUPUS 1	VEP	FEP	P300	EEG	REITAN
Normal	20%	0%	67%	60%	87%
Abnormal	80%	100%	33%	40%	13%
Total	5	8	9	10	8

LUPUS 1	VEP	FEP	P300	EEG	REITAN
Normal	25%	13%	78%	44%	77%
Abnormal	75%	88%	22%	56%	23%
Total	8	8	9	9	9

NORMALS	VEP	FEP	P300	EEG	REITAN
Normal	92%	83%	92%	86%	100%
Abnormal	8%	17%	8%	14%	0%
Total	13	12	13	14	10

TABLE III

B — Comparison among groups

	L1/L2	L1/NO	L2/NO
VEP	—	.005	.005
FEP	—	.005	.005
P300	—	—	—
EEG	—	—	.05
Reitan	—	—	—

Confidence levels are inserted according to chi square values

(— states for non significant values)

TABLE IV

Correlation among methods

	VEP					VEP				
FEP	3.43	FEP				FEP	—	FEP		
P300	—	—	P300			P300	—	—	P300	
EEG	4.44	—	—	EEG		EEG	—	—	—	EEG
REIT	—	3.43	—	—		REIT	5.0	—	—	—

— Values of chi square significant at .05 confidence level

CONCLUSIONS

These are preliminary results: Patients series are still small and EP and EEG data should be further treated specially in what concerns statistical treatment of EP mapping and EEG processing.

However the results so far obtained allow some preliminary conclusions.

Both populations, with and without previous clinical manifestations of CNS involvment had high incidence of abnormalities in FEP and in VEP. An abnormal EEG was found in a smaller precentage of cases.

As preliminary results of EP mapping it must be noted that VEP amplitudes were abnormaly high in the frontal derivations of both patient groups, mostly for P1 and for P2.

The Reitan Test and the P300 were not significantly different from the normal population.

The Reitan Test did not prove as a relevant diagnostic method. The fact that both SLE populations were without active involvment can be an explanation of these results.

Another possible explanation of the discrepancies between the results with Visual Evoked Potencials and those from tests used for evaluation of the cognitive function (P300 and Reitan B test) may be afforded by the fact these «cognitive tests» besides lack in specificity are testing functions that are not remarkably changed in neurolupus.

In general the two Lupic populations could not be distinguished from each other by the use of several neurophysiological tests.

However the occurence of major symptoms in the past introduced a higher rate of abnormal patterns in some EP modalities; namely FEP latencies were delayed in L2 population.

The high incidence of abnormal EP responses in the group without CNS symptoms may be related with systemic pathology.

The relatively small number of studied cases and the pleomorphic presentation of the disease did not allow clinical correlations.

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